d1530b

HFI-35

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food & Drug Administration
1141 Central Parkway
Cincinnati, OH 45202

November 12, 1996

WARNING LETTER
CIN-WL-97-63

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

George J. Picha, M.D.,
Chief Executive Officer
Applied Medical Technology, Inc.
6100 West Creek Road, Suite 25
Independence, Ohio 44121

Dear Dr. Picha:

During an inspection of your firm currently located in Independence, Ohio on August 19 to September 16, 1996, our investigator determined that your facility manufactures sterile gastrostomy kits. These are devices as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, and storage are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Titled 21, **Code of Federal Regulations** (CFR), Part 820.

The following deviations from Device GMP's were documented;

- Failure to conduct planned and periodic audits of the internal manufacturing, shipping and quality control program in accordance with written procedures. For example, no audits of the quality assurance program have been performed since August 1993 and of the manufacturing department since October 1994.

- Failure to conduct an audit of the contract sterilizer since July 1993 and none of the current sterilizer facility.

- Failure to maintain manufacturing and quality control procedures that are current, dated and signed. For example; fourteen of sixteen standard operating procedures reviewed were not up to date and/or not being followed and there was no written procedure for how to perform the pull test or where to record the results.

- Failure to subject specification changes in processing to controls as stringent as those applied to the original design including the approval date, the date the change becomes effective and approval by a designated individual. For example, when the mold for the 20 French Stick Peg Catheter was changed from 2 cavities to 4 cavities, the parameters (temperature, etc.) had not been validated and the change had not gone thru the established change procedure; injection times for the 18 French Domes were changed without engineering approval; tray and pouch packaging validation has not been done since starting the 100% ETO cycles; tray and packaging validation was not been done after the change in the adhesive for the trays; the 100% ETO cycle has not been validated to assure components would still be functional for at least three years after 3 sterilization cycles; no validation showing trays/pouches could be properly sterilized when much of the tyvek sheet is covered with labels and there was no data to show the packaged drugs would remain potent throughout their expiration period following three ETO cycles.

- Failure of the quality assurance program to assure that all quality assurance checks are adequate for their purpose and are performed correctly. For example, the revised SOP for inspecting trays does not include checking for burrs, holes or thin spota; there was no record showing other types of trays were investigated for burrs similar to those found in the PSMD trays; lots 96070378 and 96070399 were accepted even though the production records did not show they meet the pull test specifications and lots were accepted even though no large label was attached to the device history record.

- Failure to control environmental conditions in the packaging area prior to sealing. Other than wearing lab coats and hair/shoe covers, there were no special environmental controls to assure the product is kept clean prior to sealing. For example, the exterior door in the production area remains open; hairs and particulates are routinely found in trays/pouches and the product reworked.

- Failure to store and maintain labels in a manner that provides proper identification and assurance that prevent mixups. For example, piles of similar looking labels were stored next to each other with no spatial or physical separation. One type of label was in a tray with different labels.

- Failure to routinely calibrate production equipment. For example, pressure gauges gauge pins and one pull test gauge had not been calibrated. Another pull test gauge had not been calibrated since February 1993. The calipers had been calibrated against uncalibrated gauge pins.

- Failure to maintain complete and documented complaint files. For example, complaint follow-ups did not include reasons for why no investigations were conducted, the cause of problems and their corrections and various information on the complaints forms had not been filled out to include the assessment, the date and the person who closed the complaint.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions. The GMP deviations are similar to those noted before. Your firm received Warning Letters on GMP's in Warning Letters dated June 2, 1992 and June 10, 1993. Your firm promised and made corrections but apparently has not continued to maintain your production and quality control systems in a state of control.

In order to facilitate FDA in making the determination that permanent corrections have been made and thereby enabling FDA to withdraw its advisory to other federal agencies and to provide export clearance for products manufactured at your facility, we are requesting that you submit to this office, on the schedule below, certification by an outside expert consultant. The consultant should conduct an audit of your firm's manufacturing and quality assurance systems relative to the requirements of the device GMP regulation (21 CFR, Part 820). You should submit a copy of the consultant's report, and certification by your firm's CEO (if other than yourself) that he or she has reviewed the consultant's report and that your firm has initiated or completed all corrections called for in the report. The attached guidance may be helpful in selecting an appropriate consultant.

In our opinion, the initial certifications of audit and corrections and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by April, 1997.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates For Products For Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure injunction and/or civil penalties.

Please notify this office within 15 days of receipt of this letter, of the specific steps you will be taking to comply with our request. We are aware of your letters of September 20, 27 and October 28, 1996 which covered corrections to the FDA-483 that was issued at the close of the inspection. Please update on any additional corrections made and information on the consultant.

Your response should be sent to the Food and Drug Administration, Compliance Branch, 1141 Central Parkway, Cincinnati, Ohio 45202 to the attention of Lawrence E. Boyd, Compliance Officer.

Sincerely,

John R. Marzilli
District Director
Cincinnati District

LEB/clc